

STN

FILE 'HOME' ENTERED AT 15:35:49 ON 29 OCT 2004

L1 1046 INTERNALIZ? (4N) (ANTIBOD? OR IMMUNOGLOB? OR LIGAND?) (S) (IDENT  
IF##### OR DETERMIN? )

(FILE 'HOME' ENTERED AT 15:35:49 ON 29 OCT 2004)

FILE 'STNGUIDE' ENTERED AT 15:36:05 ON 29 OCT 2004

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, CANCERLIT' ENTERED AT  
15:37:05 ON 29 OCT 2004

L1 1046 S INTERNALIZ? (4N) (ANTIBOD? OR IMMUNOGLOB? OR LIGAND?) (S) (ID  
L2 26616 S ANTIBOD? (S) (REPORTER OR LABEL OR TAG)  
L3 22 S L1 AND L2  
L4 12 DUP REM L3 (10 DUPLICATES REMOVED)  
L5 351 S L1 AND INTERNALIZ? AND ANTIBOD?/AB  
L6 351 S L5 AND INTERNALIZ?/AB  
L7 289 S L5 AND PY<2001  
L8 159 S L5 AND (CANCER OR TUMOR? OR MALIGN?)  
L9 73 DUP REM L8 (86 DUPLICATES REMOVED)  
L10 9 S L5 AND (PHAGE-DISPLAY OR PHAGE (A) DISPLAY)  
L11 5 DUP REM L10 (4 DUPLICATES REMOVED)  
L12 70 S L9 NOT L10  
L13 68 S L9 NOT L4  
L14 51 S L13 AND L7

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2002:315065 CAPLUS  
DN 136:337344

TI Methods of high-throughput screening for internalizing ligands or  
antibodies and their receptors

IN Marks, James D.; Nielsen, Ulrik B.; Kirpotin, Dmitri B.

PA The Regents of the University of California, USA

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002033044	A2	20020425	WO 2001-US32311	20011017
	WO 2002033044	A3	20030116		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2002182643	A1	20021205	US 2001-981636	20011016
	EP 1327149	A2	20030716	EP 2001-981656	20011017
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2004526940	T2	20040902	JP 2002-536414	20011017
PRAI	US 2000-241279P	P	20001018		
	WO 2001-US32311	W	20011017		

AB This invention provides methods of **identifying ligands**  
that are **internalized** into a cell. The methods typically  
involve (i) contacting the cell with a reporter non-covalently coupled to  
a ligand; (ii) dissociating the reporter from the ligand and removing dissociated  
reporter from the surface of the cell; and (iii) detecting the reporter  
within said cell (if any is present) where the presence of the reporter  
within said cell indicates that the ligand binds to an internalizing  
receptor and is internalized.

L4 ANSWER 2 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 1

AN 2001183840 EMBASE

TI A single internalization signal from the di-leucine family is critical for  
constitutive endocytosis of the type II TGF- $\beta$  receptor.

AU Ehrlich M.; Shimueley A; Henis Y.I.

CS Y.I. Henis, Department of Neurobiochemistry, The George S. Wise Fac. of  
Life Sci., Tel Aviv University, Tel Aviv 69978, Israel.  
henis@post.tau.ac.il

SO Journal of Cell Science, (2001) 114/9 (1777-1786).

Refs: 64

ISSN: 0021-9533 CODEN: JNCSAI

CY United Kingdom

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB Endocytosis has an important contribution to the regulation of the surface  
expression levels of many receptors. In spite of the central role of the

transforming growth factor  $\beta$  (TGF- $\beta$ ) receptors in numerous cellular and physiological processes, their endocytosis is largely unexplored. Current information on TGF- $\beta$  receptor endocytosis relies exclusively on studies with chimeric constructs containing the extracellular domain of the GMCSF receptors, following the **internalization** of the GMCSF **ligand**; the conformation and interactions of the chimeric receptors (and therefore their endocytosis) may differ considerably from those of the native TGF- $\beta$  receptors. Furthermore, there are no data on the potential endocytosis motif(s) of the TGF- $\beta$  receptors or other receptor Ser/Thr kinases. Here, we report the use of type II TGF- $\beta$  receptors, myc-tagged at their extracellular terminus, to investigate their endocytosis. Employing fluorescent **antibody** fragments to **label** exclusively the cell surface myc-tagged receptors exposed to the external milieu, made it possible to follow the internalization of the receptors, without the complications that render labeling with TGF- $\beta$  (which binds to many cellular proteins) unsuitable for such studies. The results demonstrate that the full-length type II TGF- $\beta$  receptor undergoes constitutive endocytosis via clathrin-coated pits. Using a series of truncation and deletion mutants of this receptor, we **identified** a short peptide sequence (I(218)I(219)L(220)), which conforms to the consensus of internalization motifs from the di-leucine family, as the major endocytosis signal of the receptor. The functional importance of this sequence in the full-length receptor was validated by the near complete loss of internalization upon mutation of these three amino acids to alanine.

L4 ANSWER 3 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
AN 2000:478782 SCISEARCH  
GA The Genuine Article (R) Number: 325ZB  
TI A screen of random sequences for those that alter the trafficking of the  
influenza virus hemagglutinin in vivo  
AU Lewis C M; Latham K; Roth M G (Reprint)  
CS UNIV TEXAS, SW MED CTR, DEPT BIOCHEM, DALLAS, TX 75235 (Reprint); UNIV  
TEXAS, SW MED CTR, DEPT BIOCHEM, DALLAS, TX 75235  
CYA USA  
SO TRAFFIC, (MAR 2000) Vol. 1, No. 3, pp. 282-290.  
Publisher: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016  
COPENHAGEN, DENMARK.  
ISSN: 1398-9219.  
DT Article; Journal  
FS LIFE  
LA English  
REC Reference Count: 52  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In order to **determine** if the sequence patterns known to specify internalization represent the majority of possible internalization signals, we **identified** random sequences capable of causing a **reporter** protein to be internalized at least several-fold faster than the rate of non-selective internalization of membrane by clathrin-coated pits. A library of influenza hemagglutinin (HA) proteins, bearing short random sequences in place of the wild-type cytoplasmic domain, was prepared in recombinant SV40 virus. The library was expressed and screened for HAs that could **internalize** anti-HA **antibody** from the medium. The cytoplasmic sequences of the selected proteins were **determined**. From a small sample of sequences, we detected several that did not resemble those previously **identified**. The known internalization signals must represent only a subset of the sequences that can serve as internalization signals.

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1999:709004 CAPLUS  
 DN 131:321545  
 TI Methods of selecting internalizing antibodies  
 IN Marks, James D.; Poul, Marie-alix; Becerril, Baltazar  
 PA The Regents of the University of California, USA  
 SO PCT Int. Appl., 88 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9956129	A1	19991104	WO 1999-US8468	19990422
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2001008759	A1	20010719	US 1999-249529	19990212
	US 6794128	B2	20040921		
	CA 2326499	AA	19991104	CA 1999-2326499	19990422
	AU 9938622	A1	19991116	AU 1999-38622	19990422
	AU 768784	B2	20040108		
	EP 1073905	A1	20010207	EP 1999-921396	19990422
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2002513156	T2	20020508	JP 2000-546239	19990422
PRAI	US 1998-82953P	P	19980424		
	US 1999-249529	A	19990212		
	WO 1999-US8468	W	19990422		
AB	This invention provides methods of selecting antibodies that are internalized into target cells. The methods generally involve contacting target cells with one or more members of an antibody phage display library, shown in the figure. The members of the phage display library are also contacted with cells of subtractive cell line. The target cells are then washed to remove the subtractive cell line cells and members of phage display library that are non-specifically bound or weakly bound to the target cells. The target cells are cultured under conditions where members of the phage display library can be internalized if bound to an internalizing marker and internalized members of the phage display library are then identified.				
RE.CNT	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT			

L4 ANSWER 5 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 1999367258 EMBASE  
 TI Studies on the red marrow dosimetry in radioimmunotherapy: An experimental investigation of factors influencing the radiation-induced myelotoxicity in therapy with  $\beta$ -, auger/conversion electron-, or  $\alpha$ -emitters.  
 AU Behr T.M.; Sgouros G.; Stabin M.G.; Behe M.; Angerstein C.; Blumenthal R.D.; Apostolidis C.; Molinet R.; Sharkey R.M.; Koch L.; Goldenberg D.M.; Becker W.  
 CS T.M. Behr, Department of Nuclear Medicine, Georg-August-University of Gottingen, Robert-Koch-Strasse 40, D-37075 Gottingen, Germany.  
 tmbehr@med.uni-goettingen.de

SO Clinical Cancer Research, (1999) 5/10 SUPPL. (3031s-3043s).

Refs: 54

ISSN: 1078-0432 CODEN: CCREF4

CY United States

DT Journal; Conference Article

FS 016 Cancer

023 Nuclear Medicine

025 Hematology

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LA English

SL English

AB Usually, the red marrow (RM) is the first dose-limiting organ in radioimmunotherapy. However, several studies have obtained only poor correlations between the marrow doses and the resulting toxicities. Furthermore, RM doses are mostly not **determined** directly but are derived from blood doses by assuming a ratio that is, over time for the respective conjugates, more or less constant between blood and marrow activities. The aim of this study was to **determine**, in a mouse model, this RM:blood activity ratio for various immunoconjugates, to investigate whether there may be differences between complete IgG and its fragments with various **labels** (125/131I versus 111In, (88/90)Y, or 213Bi), and to analyze, in more detail, factors other than just total dose, such as dose rate or relative biological effectiveness factors, that may influence the resulting myelotoxicity. The maximum tolerated activities (MTAs) and doses (MTDs) of several murine, chimeric, and humanized immunoconjugates as complete IgG or fragments (F(ab)2 and Fab), labeled with  $\beta$ emitters (such as 131I or 90Y), Auger electron-emitters (such as 125I or 111In), or  $\alpha$ -emitters (such as 213Bi) were **determined** in nude mice. Blood counts were monitored at weekly intervals; bone marrow transplantation was performed to support the assumption of the RM as dose-limiting. The radiation dosimetry was derived from biodistribution data of the various conjugates, accounting for cross-organ radiation; besides the major organs, the activities in the blood and bone marrow (and bone) were **determined** over time. Whereas no significant differences were found for the RM:blood ratios between various IgG subtypes, different radiolabels or various time points, differences were found between IgG and bi- or monovalent fragments: typically, the RM:blood ratios were approximately 0.4 for IgG, 0.8 for F(ab')2, and 1.0 for Fab'. Nevertheless, at the respective MTAs, the RM doses differed significantly between the three conjugates: e.g., with 131I-labeled conjugates, the maximum tolerated activities were 260  $\mu$ Ci for IgG, 1200  $\mu$ Ci for F(ab)2, and 3 mCi for Fab, corresponding to blood doses of 17, 9, and 4 Gy, respectively. However, initial dose rates were 10 times higher with Fab as compared to IgG, and still 3 times higher as compared to F(ab)2; interestingly, all three deliver .apprx.4 Gy within the first 24 h. The MTDs of all three conjugates were increased by BMT by approximately 30%. Similar observations were made for 90Y- conjugates. Higher RM doses were tolerated with Auger-emitters than with conventional  $\beta$ emitters, whereas the MTDs were similar between  $\alpha$ - and  $\beta$ emitters. In accordance to dose rates never exceeding those occurring at the single injection MTA, two subsequent injections of two doses of 80% of the single shot MTA of 131I- or 90Y-labeled Fab' and two doses of 100% of the single shot MTA of 213Bi-labeled Fab' were tolerated without increased lethality, if administered 24-48 h apart. In contrast, reinjection of bivalent conjugates was not possible within 6 weeks. These data suggest that the RM:blood activity ratios differ between IgG and fragments, although there is no anatomical or physiological explanation for this phenomenon at this point. In contrast to the current opinion, indication for a strong influence of the dose rate (or dose per unit time), not only total dose, on the resulting toxicity is provided, whereas

the influence of high-linear energy transfer ( $\alpha$  and Auger/conversion electrons) versus low-linear energy transfer ( $\beta$  and  $\gamma$ ) type radiation seems to be much lower than expected from previous in vitro data. The lower myelotoxicity of Auger-emitters is probably due to the short path length of their low-energy electrons, which cannot reach the nuclear DNA if the **antibody** is not **internalized** into the stem cells of the RM.

- L4 ANSWER 6 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 2
- AN 1999340545 EMBASE
- TI The Menkes protein (ATP7A; MNK) cycles via the plasma membrane both in basal and elevated extracellular copper using a C-terminal di-leucine endocytic signal.
- AU Petris M.J.; Mercer J.F.B.
- CS J.F.B. Mercer, Centre Cellular Molecular Biology, School Biological Chemical Sciences, Deakin University, 221 Burwood Highway, Burwood, Vic. 3125, Australia. jmercer@deakin.edu.au
- SO Human Molecular Genetics, (1999) 8/11 (2107-2115).  
Refs: 31  
ISSN: 0964-6906 CODEN: HMGEE5
- CY United Kingdom
- DT Journal; Article
- FS 022 Human Genetics  
029 Clinical Biochemistry
- LA English
- SL English
- AB Menkes disease is an X-linked recessive copper deficiency disorder caused by mutations in the ATP7A (MNK) gene which encodes a copper transporting P-type ATPase (MNK). MNK is normally localized predominantly in the trans-Golgi network (TGN); however, when cells are exposed to excessive copper it is rapidly relocalized to the plasma membrane where it functions in copper efflux. In this study, the c-myc epitope was introduced within the loop connecting the first and second transmembrane regions of MNK. This myc epitope allowed detection of the protein at the surface of living cells and provided the first experimental evidence supporting the common topological model. In cells stably expressing the tagged MNK protein (MNK-**tag**), extracellular **antibodies** were **internalized** to the perinuclear region, indicating that MNK-**tag** at the TGN constitutively cycles via the plasma membrane in basal copper conditions. Under elevated copper conditions, MNK-**tag** was recruited to the plasma membrane; however, internalization of MNK-**tag** was not inhibited and the protein continued to recycle through cytoplasmic membrane compartments. These findings suggest that copper stimulates exocytic movement of MNK to the plasma membrane rather than reducing MNK retrieval and indicate that MNK may remove copper from the cytoplasm by transporting copper into the vesicles through which it cycles. Newly internalized MNK-**tag** and transferrin were found to co-localize, suggesting that MNK-**tag** follows a clathrin-coated pit/endosomal pathway into cells. Mutation of the di-leucine, L1487 L1488, prevented uptake of anti-myc **antibodies** in both basal and elevated copper conditions, thereby **identifying** this sequence as an endocytic signal for MNK. Analysis of the effects of the di-leucine mutation in elevated copper provided further support for copper-stimulated exocytic movement of MNK from the TGN to the plasma membrane.
- L4 ANSWER 7 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3
- AN 1999004233 EMBASE
- TI Neuronal nicotinic acetylcholine receptors in rat trigeminal ganglia.
- AU Liu L.; Chang G.-Q.; Jiao Y.Q.; Simon S.A.

CS S.A. Simon, Dept. of Neurobiology/Anesthesiology, Duke University Medical Center, Durham, NC 27710, United States. sas@neuro.duke.edu

SO Brain Research, (2 Nov 1998) 809/2 (238-245).  
 Refs: 38  
 ISSN: 0006-8993 CODEN: BRREAP

PUI S 0006-8993(98)00862-2

CY Netherlands

DT Journal; Article

FS 008 Neurology and Neurosurgery

LA English

SL English

AB The application of nicotine to the various epithelia served by the trigeminal nerve produces irritation and/or pain by activating neuronal nicotinic acetylcholine receptors (NnAChRs) in sensory neurons. In this study the NnAChRs were **identified** in rat trigeminal ganglia (TG) using RT-PCR and immunocytochemistry. With RT-PCR the subunits of NnAChRs in rat TG were **determined**, and with immunocytochemistry the localization of three prominent subunits ( $\alpha 7$ ,  $\alpha 4$  and  $\beta 2$ ) were localized in intact TG neurons. The relative abundance of the  $\alpha$  and  $\beta$  subunits were:  $\alpha 7$  .simeq.  $\alpha 3 > \alpha 6 > \alpha 4$  .simeq.  $\alpha 5 > \alpha 9 \geq \alpha 2$ , and  $\beta 2$  .simeq.  $\beta 3 > \beta 4$ . This is the first report of the  $\alpha 9$  subunit in TG. Immunohistochemical studies revealed that almost all TG neurons contained  $\alpha 7$ -LI and  $\alpha 4$ -LI, and that 85% had  $\beta 2$ -LI. For these three subunits much of the **label** was **internalized**. Immunocytochemical studies using **antibodies** raised against chick  $\alpha 8$  subunits did not specifically **label** rat TG. These data reveal that rat TG neurons contain the entire spectrum of mammalian NnAChR subunits.

L4 ANSWER 8 OF 12 CANCERLIT on STN

AN 1998638677 CANCERLIT

DN 98638677

TI Auger-electron versus beta-emitters in radioimmunotherapy (RIT) of human colon cancer xenografts in comparison to standard chemotherapy (Meeting abstract).

AU Anonymous

CS Depts. of Nuclear Medicine and Radiation Oncology, University of Gottingen, D-37075, Germany.

SO Proc Annu Meet Am Assoc Cancer Res, (1997) 38 A1677.  
 ISSN: 0197-016X.

DT (MEETING ABSTRACTS)

LA English

FS Institute for Cell and Developmental Biology

EM 199807

ED Entered STN: 19980713  
 Last Updated on STN: 19980713

AB Recent clinical results suggest higher anti-tumor efficacy of **internalizing** monoclonal **antibodies** (MAbs) at lower toxicity when labeled with Auger-electron emitters as compared to conventional beta-emitters. The aim of this study was to compare the toxicity and anti-tumor efficacy of the 125I- and 131I-labeled internalizing MAb, 17-1A, to conventional chemotherapy with 5-fluorouracil/leucovorin (5-FU/LV) in human colon cancer xenografted nude mice. The mice were left untreated, injected either with unlabeled, 125I- or 131I-labeled MAb, or were given 5-FU/LV. The maximum tolerated doses (MTD) were **determined**, without artificial support or with bone marrow transplantation (BMT). Toxicity was monitored. Whereas cold 17-1A was inert, the MTDs of 131I- and 125I-17-1A without artificial support were 300 uCi and 3 mCi, respectively. Myelotoxicity was dose-limiting. BMT enabled dose-intensification to 400 uCi with 131I-**label**, whereas

the MTD of 125I-17-1A with BMT has not been reached at 5 mCi. The MTD of 5-FU/LV was 0.6/1.8 mg/d x 5d. BMT was unable to increase this MTD, suggesting mucositis to be dose-limiting. Whereas no anti-tumor effects were seen with cold 17-1A and the effects of 5-FU/LV were minimal, tumor growth was retarded with 131I-17-1A. With 125I-**label** however, partial remissions (greater than or equal to 50% tumor volume reduction) occurred at 3 mCi, complete remissions at 5 mCi. These data suggest the superiority of Auger-emitters, such as 125I, as compared to conventional beta-emitters in RIT with internalizing MABs at equitoxic doses. Furthermore, higher anti-tumor efficacy of RIT as compared to chemotherapy is indicated.

L4 ANSWER 9 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 4  
AN 97197686 EMBASE  
DN 1997197686  
TI Advantage of residualizing radiolabels for an internalizing antibody  
against the B-cell lymphoma antigen, CD22.  
AU Sharkey R.M.; Behr T.M.; Mattes M.J.; Stein R.; Griffiths G.L.; Shih L.B.;  
Hansen H.J.; Blumenthal R.D.; Dunn R.M.; Juweid M.E.; Goldenberg D.M.  
CS D.M. Goldenberg, Garden State Cancer Center, 520 Belleville Avenue,  
Belleville, NJ 07109, United States  
SO Cancer Immunology Immunotherapy, (1997) 44/3 (179-188).  
Refs: 47  
ISSN: 0340-7004 CODEN: CIIMDN  
CY Germany  
DT Journal; Article  
FS 016 Cancer  
025 Hematology  
026 Immunology, Serology and Transplantation  
037 Drug Literature Index  
LA English  
SL English  
AB LL2 is an anti-CD22 pan-B-cell monoclonal **antibody** which, when  
radiolabeled, has a high sensitivity for detecting B-cell, non-Hodgkin's  
lymphoma (NHL), as well as an antitumor efficacy in therapeutic  
applications. The aim of this study was to **determine** whether  
intracellularly retained radiolabels have an advantage in the diagnosis  
and therapy of lymphoma with LL2. In vitro studies showed that iodinated  
LL2 is intracellularly catabolized, with a rapid release of the  
radioiodine from the cell. In contrast, residualizing radiolabels, such as  
radioactive metals, are retained intracellularly for substantially longer.  
In vivo studies were performed using LL2-labeled with radioiodine by a  
non-residualizing (chloramine-T) or a residualizing method  
(dilactitol-tyramine, DLT), or with a radioactive metal (111In). The  
biodistribution of a mixture of 125I (non-residualizing chloramine-T  
compared to residualizing DLT), 111In-labeled LL2 murine IgG2a or its  
fragments [F(ab')<sub>2</sub>, Fab'], as well as its humanized, CDR- grafted form,  
was studied in nude mice bearing the RL human B-cell NHL cell line.  
Radiation doses were calculated from the biodistribution data according to  
the Medical International Radiation Dose scheme to assess the potential  
advantage for therapeutic applications. At all assay times, tumor uptake  
was higher with the residualizing **labels** (i.e., 111In and  
DLT-125I) than with the non-residualizing iodine **label**. For  
example, tumor/blood ratios of 111In-labeled IgG were 3.2-, 3.5- and  
2.8-fold higher than for non- residualizing iodinated IgG on days 3, 7 and  
14, respectively. Similar results were obtained for DLT-labeled IgG and  
fragments with residualized radiolabels. Tumor/organ ratios also were  
higher with residualizing **labels**. No significant differences in  
tumor, blood and organ uptake were observed between murine and humanized  
LL2. The conventionally iodinated anti-CD20 **antibody**, 1F5, had

tumor uptake values comparable to those of iodinated LL2, the uptake of both anti-bodies being strongly dependent on tumor size. These data suggest that, with **internalizing antibodies** such as LL2, labeling with intracellularly retained isotopes has an advantage over released ones, which justifies further clinical trials with residualizing <sup>111</sup>In-labeled LL2 for diagnosis, and residualizing <sup>131</sup>I and <sup>90</sup>Y **labels** for therapy.

L4 ANSWER 10 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 5

AN 95289295 EMBASE

DN 1995289295

TI Tumor-specific anti-epidermal growth factor receptor variant III monoclonal antibodies: Use of the tyramine-cellobiose radioiodination method enhances cellular retention and uptake in tumor xenografts.

AU Reist C.J.; Archer G.E.; Kurpad S.N.; Wikstrand C.J.; Vaidyanathan G.; Willingham M.C.; Moscatello D.K.; Wong A.J.; Bigner D.D.; Zalutsky M.R.

CS Department of Radiology, Duke University Medical Center, Box 3808, Durham, NC 27710, United States

SO Cancer Research, (1995) 55/19 (4375-4382).

ISSN: 0008-5472 CODEN: CNREA8

CY United States

DT Journal; Article

FS 016 Cancer

037 Drug Literature Index

LA English

SL English

AB Amplification and rearrangement of the epidermal growth factor receptor (EGFR) gene are characteristics of many types of tumors. One class of EGFR mutations, EGFRvIII, is characterized by an in-frame deletion resulting in a truncated external domain of the receptor. EGFR-viii was first **identified** in a subset of gliomas and has since been found in some non-small cell lung carcinomas and breast carcinomas. mAbs specific for this variant form of EGFR but unreactive with the wild-type EGFR have been reported from our laboratory. This study further characterizes three of these **antibodies**. We **determined**, via radiolabeling techniques and immunofluorescence microscopy, that, after cell binding in vitro, the anti-EGFRvIII-specific mAbs internalize at 37°C. Furthermore, subsequent to **internalization**, the **antibodies** were processed intracellularly, presumably by lysosomal degradation. We also examined the use of an alternative radiolabeling procedure that uses nonmetabelizable radioiodinated tyramine cellobiose. Our results show that the tyramine cellobiose labeling method allows for greater tumor cell retention of radiolabel in vitro (76% for tyramine cellobiose and 27% for Iodo-Gen after 24 h). Paired-**label** biodistribution studies in athymic mice indicate that anti-EGFRvIII mAb L8A4 localizes specifically to EGFRvIII- expressing tumor xenografts with a maximum of 34.3 ± 7.6% injected dose/g when labeled using tyramine cellobiose compared with a maximum of 14.9 ± 4.3% injected dose/g using Iodo-Gen; similar results were obtained with mAb H10. These results suggest that the anti-EGFRvIII mAbs may serve as potential carriers for radioconjugate- and immunotoxin-based therapies for tumors expressing EGFRvIII.

L4 ANSWER 11 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 6

AN 95026278 EMBASE

DN 1995026278

TI Quantitative measurement of α6β1 and α6β4 integrin internalization under cross-linking conditions: A possible role for α6 cytoplasmic domains.

AU Gaietta G.; Redelmeier T.E.; Jackson M.R.; Tamura R.N.; Quaranta V.  
 CS Department of Cell Biology, The Scripps Research Institute, 10666 North  
 Pines Road, La Jolla, CA 92037, United States  
 SO Journal of Cell Science, (1994) 107/12 (3339-3349).  
 ISSN: 0021-9533 CODEN: JNCSAI  
 CY United Kingdom  
 DT Journal; Article  
 FS 029 Clinical Biochemistry  
 LA English  
 SL English  
 AB In epithelial cells integrins are segregated on discrete domains of the  
 plasma membrane. Redistribution may also occur during migration or  
 differentiation. However, little is known about the mechanisms that  
 control such redistribution. Receptor internalization may be a part of one  
 such mechanism. We developed a quantitative assay and measured  
 internalization of two epithelial integrin heterodimers,  $\alpha 6 \beta 1$   
 and  $\alpha 6 \beta 4$ , induced by cross-linking with specific  
**antibodies**.  $\alpha 6 \beta 1$  is a receptor for EHS laminin, while  
 $\alpha 6 \beta 4$  is a receptor for a component of the basement membrane.  
 $\alpha 6 \beta 4$  plays an important role in the establishment of  
 hemidesmosomes, and becomes redistributed on the epithelial cell surface  
 when cells are in a migratory phase. We report that  $\alpha 6 \beta 4$  is  
 efficiently internalized in human keratinocytes. More than 25% of cell  
 surface  $\alpha 6 \beta 4$  was internalized at 30 minutes, after  
 cross-linking with A9, an anti- $\beta 4$  monoclonal **antibody**.  
 $\alpha 6 \beta 1$  is also internalized, in melanoma and teratocarcinoma  
 cells, with maximum values of 20% of total receptors expressed at the cell  
 surface. No significant difference was observed between the  $\alpha 6$   
 isoforms A and B in these assays. To **determine** whether  $\alpha 6$   
 cytoplasmic domains could influence integrin endocytosis, we prepared  
 chimeric constructs with the extracellular domain of a **reporter**  
 protein (CD8), and the cytoplasmic domains of either  $\alpha 6 A$  or  
 $\alpha 6 B$ . Both  $\alpha 6$  cytoplasmic domains but not a control cytoplasmic  
 domain promoted internalization of the chimeric proteins, after  
 cross-linking with **antibody**. **Internalization** of  
 $\alpha 6$  integrins may have a role in redistributing these receptors at  
 the cell surface. Furthermore, the cytoplasmic domains of  $\alpha 6$  may be  
 involved in regulating integrin internalization.

L4 ANSWER 12 OF 12 CANCERLIT on STN  
 AN 94031446 CANCERLIT  
 DN 94031446 PubMed ID: 8105852  
 TI Treatment of leukemia with radiolabeled monoclonal antibodies.  
 AU Sgouros G; Scheinberg D A  
 CS Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New  
 York, NY 10021.  
 SO CANCER TREATMENT AND RESEARCH, (1993) 68 23-64. Ref: 132  
 Journal code: 8008541. ISSN: 0927-3042.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS MEDLINE; Priority Journals  
 OS MEDLINE 94031446  
 EM 199312  
 ED Entered STN: 19941107  
 Last Updated on STN: 19941107  
 AB In contrast to radioimmunotherapy of solid disease, wherein the primary  
 obstacle to success is access of radiolabeled **antibody** to  
 antigen-positive cells, in the treatment of leukemia delivering a lethal

absorbed dose to the isolated cell appears to be the primary obstacle. The isolated cell is defined as one that is exposed only to self-irradiation (from **internalized** or surface-bound radiolabeled **antibody**) and to irradiation from free **antibody** in the blood. It is isolated in the sense that the particulate (beta, electron, alpha) emissions from its nearest neighboring antigen-positive cell do not contribute to its absorbed dose. Disease in the bone marrow and other tissues, since it is confined to a smaller volume, is more easily eradicated because the absorbed dose to a given cell nucleus is enhanced by emissions from adjacent cells (a smaller fraction of the emission energy is 'wasted'). The optimization simulations presented above for the M195 **antibody** suggest that the optimum dose of **antibody** that should be administered is that required to yield a concentration within the distribution volume of the **antibody** that is approximately equal to the concentration of antigen sites as **determined** by the tumor burden. Although not specifically considered in the modeling example presented above, **antibody internalization** and catabolism may be expected to play an important role in radioimmunotherapy treatment planning of leukemia. Depending upon the kinetics of internalization and catabolism, the absorbed dose to the red marrow and to antigen-positive cells may be reduced considerably, since catabolism, assuming that it is followed by rapid extrusion of the radioactive **label**, would decrease the cells' exposure time considerably. The recently demonstrated effectiveness of radioimmunotherapy in certain cases of B-cell lymphoma and in reducing tumor burden in acute myelogenous leukemia suggests that radioimmunotherapy is beginning to fulfill the promise held when it was initially conceived. The long delay in achieving reproducible success has, in large part, been the result of the conceptual simplicity of using agents that specifically 'target' tumor cells and they may thus selectively deliver cytotoxic agents. Emboldened by this apparent simplicity, early trials of radioimmunotherapy failed to consider the many variables involved in its implementation. As has been recently demonstrated using mathematical models of **antibody** delivery to solid tumor, chief among these may have been the failure to select the appropriate tumor type. By significantly reducing the problems associated with **antibody** delivery, hematopoietic malignancies offer the optimum conditions for successful radioimmunotherapy. As evinced by the wide range of **antibody** and radioactivity doses administered in the B-cell lymphoma trials, the case-specific nature of radioimmunotherapy requires an understanding of the relationship between the various input parameters and patient response. The complexity and interrelationship of these parameters precludes an experimental trial-and-error approach to their optimization. A stepwise approach to radioimmunotherapy treatment planning is proposed in which a model of **antibody** kinetics is developed and validated. (ABSTRACT TRUNCATED AT 400 WORDS)

L11 ANSWER 1 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 1

AN 2004043851 EMBASE

TI Mapping Tumor Epitope Space by Direct Selection of Single-Chain Fv  
Antibody Libraries on Prostate Cancer Cells.

AU Liu B.; Conrad F.; Cooperberg M.R.; Kirpotin D.B.; Marks J.D.

CS B. Liu, Department of Anesthesia, 1001 Potrero Avenue, San Francisco, CA  
94110, United States. Liub@anesthesia.ucsf.edu

SO Cancer Research, (15 Jan 2004) 64/2 (704-710).  
Refs: 38  
ISSN: 0008-5472 CODEN: CNREA8

CY United States

DT Journal; Article

FS 016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy

LA English

SL English

AB The **identification** of tumor-specific cell surface antigens is a critical step toward the development of targeted therapeutics for cancer. The epitope space at the tumor cell surface is highly complex, composed of proteins, carbohydrates, and other membrane-associated **determinants** including post-translational modification products, which are difficult to probe by approaches based on gene expression. This epitope space can be efficiently mapped by complementary monoclonal **antibodies**. By selecting human **antibody** gene diversity libraries directly on the surface of prostate cancer cells, we have taken a functional approach to **identifying** fully human, tumor-specific monoclonal **antibodies** without prior knowledge of their target antigens. Selection conditions have been optimized to favor tumor-specific **antibody** binding and **internalization**. To date, we have discovered >90 monoclonal **antibodies** that specifically bind and enter prostate cancer cells, with little or no binding to control cells. These **antibodies** are able to efficiently deliver intracellular payloads when attached to nanoparticles such as liposomes. In addition, a subset of the **antibodies** displayed intrinsic antiproliferative activity. These tumor-specific **internalizing antibodies** are likely to be useful for targeted therapeutics either alone or in combination with effector molecules. The antigens they bind constitute a tumor-specific **internalizing** epitope space that is likely to play a significant role in cancer cell homeostasis. Targeting components of this epitope space may facilitate development of immunotherapeutic and small molecule-based strategies as well as the use of other therapeutic agents that rely upon delivery to the interior of the tumor cell.

L11 ANSWER 2 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 2

AN 2004322839 EMBASE

TI Selection of **internalizing** ligand-**display**  
**phage** using rolling circle amplification for phage recovery.

AU Burg M.; Ravey E.P.; Gonzales M.; Amburn E.; Faix P.H.; Baird A.; Larocca D.

CS Dr. D. Larocca, Selective Genetics, Inc., 11588 Sorrento Valley Road, San  
Diego, CA 92121, United States. laroccad@cox.net

SO DNA and Cell Biology, (2004) 23/7 (457-462).  
Refs: 22  
ISSN: 1044-5498 CODEN: DCEBE8

CY United States

DT Journal; Article

FS 021 Developmental Biology and Teratology  
 029 Clinical Biochemistry  
 LA English  
 SL English  
 AB Selection of phage libraries against complex living targets such as whole cells or organs can yield valuable targeting ligands without prior knowledge of the targeted receptor. Our previous studies have shown that noninfective multivalent **ligand** display phagemids **internalize** into mammalian cells more efficiently than their monovalent counterparts suggesting that cell-based selection of **internalizing ligands** might be improved using multivalently displayed peptides, **antibodies** or cDNAs. However, alternative methods of phage recovery are needed to select phage from noninfective libraries. To this end, we reasoned that rolling circle amplification (RCA) of phage DNA could be used to recover noninfective phage. In feasibility studies, we obtained up to 1.5 million-fold enrichment of **internalizing** EGF-targeted phage using RCA. When RCA was applied to a large random peptide library, eight distinct human prostate carcinoma cell-**internalizing** peptides were isolated within three selection rounds. These data establish RCA as an alternative to infection for phage recovery that can be used to **identify** peptides from noninfective **phage display** libraries or infective libraries under conditions where there is the potential for loss of phage infectivity.

L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2002:711314 CAPLUS  
 DN 137:227660  
 TI Methods using genetic package (e.g. **phage**) **display** for selecting **internalizing** ligands (e.g. drugs) for gene delivery  
 IN Larocca, David; Baird, Andrew; Kassner, Paul  
 PA Selective Genetics, Inc., USA  
 SO U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 193,445.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6451527	B1	20020917	US 1999-258689	19990226
	US 6472146	B1	20021029	US 1998-195379	19981117
	US 6589730	B1	20030708	US 1998-193445	19981117
	CA 2352463	AA	20000525	CA 1999-2352463	19991029
	WO 2000029555	A1	20000525	WO 1999-US25361	19991029
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2000013299	A5	20000605	AU 2000-13299	19991029
	EP 1133553	A1	20010919	EP 1999-956763	19991029
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2002068272	A1	20020606	US 2001-866073	20010524
	US 6723512	B2	20040420		
	US 2003148263	A1	20030807	US 2002-151204	20020517
PRAI	US 1997-57067P	P	19970829		

US 1998-141631	B2	19980828
US 1998-193445	A2	19981117
US 1998-195379	A2	19981117
US 1999-258689	A	19990226
WO 1999-US25361	W	19991029
US 2001-866073	A2	20010524

AB This invention relates generally to genetic package display (e.g., **phage display**), and in particular, to selection of ligands that bind to a cell surface receptor and **internalize**. A genetic package display system is presented for selecting **internalizing** ligands for gene delivery. The genetic package carries a reporter, selectable marker, or a specifically detectable nucleic acid sequence and presents a ligand on its surface. A library of potential ligands may be screened for the ability to successfully transduce target cells. Within one aspect of the present invention, a method of selecting **internalizing** ligands displayed on a genetic package is presented, comprising: (a) contacting a ligand displaying genetic package(s) with a cell(s), wherein the package carries a gene encoding a detectable product which is expressed upon **internalization** of the package; and (b) detecting product expressed by the cell(s); thereby selecting **internalizing** ligands displayed on a genetic package. In one embodiment of the present invention, a library of **antibodies**, cDNAs, or genes encoding random peptides is cloned into a coat protein (e.g., gene III protein of filamentous phage) of a bacteriophage. The phage genome also contains an "expression cassette" encoding a transgene placed downstream from a cell promoter that is active in the cells to be infected. The transgene is generally a selectable gene product and/or a detectable marker. The cells may be isolated on the basis of transgene expression. The gene(s) that are fused with the coat protein and that promoted cell binding and **internalization** are recovered from the selected cells by a suitable method. The therapeutic gene product is selected from the group consisting of protein, ribozyme, and antisense oligonucleotide, and in other embodiments the therapeutic gene product is a cytotoxic agent (e.g., ribosome inactivating protein), or is an **antibody** that binds to HER2/neu. The construction of the **phage display** vector containing FGF2 was demonstrated as well as the transduction of mammalian cells by FGF2-ligand **display phage**.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:709004 CAPLUS  
DN 131:321545  
TI Methods of selecting **internalizing** antibodies  
IN Marks, James D.; Poul, Marie-alix; Becerril, Baltazar  
PA The Regents of the University of California, USA  
SO PCT Int. Appl., 88 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9956129	A1	19991104	WO 1999-US8468	19990422
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,  
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,  
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001008759	A1	20010719	US 1999-249529	19990212
US 6794128	B2	20040921		
CA 2326499	AA	19991104	CA 1999-2326499	19990422
AU 9938622	A1	19991116	AU 1999-38622	19990422
AU 768784	B2	20040108		
EP 1073905	A1	20010207	EP 1999-921396	19990422

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

JP 2002513156	T2	20020508	JP 2000-546239	19990422
PRAI US 1998-82953P	P	19980424		
US 1999-249529	A	19990212		
WO 1999-US8468	W	19990422		

AB This invention provides methods of selecting **antibodies** that are **internalized** into target cells. The methods generally involve contacting target cells with one or more members of an **antibody phage display** library, shown in the figure. The members of the **phage display** library are also contacted with cells of subtractive cell line. The target cells are then washed to remove the subtractive cell line cells and members of **phage display** library that are non-specifically bound or weakly bound to the target cells. The target cells are cultured under conditions where members of the **phage display** library can be **internalized** if bound to an **internalizing** marker and **internalized** members of the **phage display** library are then identified.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

AN 1999:140208 CAPLUS

DN 130:310320

TI Toward selection of **internalizing** antibodies from phage libraries

AU Becerril, Baltazar; Poul, Marie-Alix; Marks, James D.

CS Department of Anesthesia, University of California, San Francisco, San Francisco, CA, 94110, USA

SO Biochemical and Biophysical Research Communications (1999), 255(2), 386-393

CODEN: BBRCA9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

AB **Antibodies** which bind cell surface receptors in a manner whereby they are endocytosed are useful mols. for the delivery of drugs, toxins, or DNA into the cytosol of mammalian cells for therapeutic applications. Traditionally, **internalizing antibodies** have been **identified** by screening hybridomas. For this work, the authors studied a human scFv (C6.5) which binds ErbB2 to **det.** the feasibility of directly selecting **internalizing antibodies** from phage libraries and to **identify** the most efficient display format. Using wild-type C6.5 scFv displayed monovalently on a phagemid, the authors demonstrate that anti-ErbB2 phage **antibodies** can undergo receptor-mediated endocytosis. Using affinity mutants and dimeric diabodies of C6.5 displayed as either single copies on a phagemid or multiple copies on phage, the authors define the role of affinity, valency, and display format on phage endocytosis and identify the factors that lead to the greatest enrichment for **internalization**. Phage displaying bivalent diabodies or multiple

copies of scFv were more efficiently endocytosed than phage displaying monomeric scFv and recovery of infectious phage was increased by preincubation of cells with chloroquine. Measurement of phage recovery from within the cytosol as a function of applied phage titer indicates that it is possible to select for endocytosable **antibodies**, even at the low concns. that would exist for a single phage **antibody** member in a library of 10<sup>9</sup>. (c) 1999 Academic Press.

RE.CNT 29      THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 51 MEDLINE on STN  
 AN 1999160873 MEDLINE  
 DN PubMed ID: 10049718  
 TI Toward selection of **internalizing** antibodies from phage libraries.  
 AU Becerril B; Poul M A; Marks J D  
 CS Department of Pharmaceutical Chemistry, University of California, San Francisco 94110, USA.  
 SO Biochemical and biophysical research communications, (1999 Feb 16) 255 (2) 386-93.  
 Journal code: 0372516. ISSN: 0006-291X.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199903  
 ED Entered STN: 19990324  
 Last Updated on STN: 20000303  
 Entered Medline: 19990311

L14 ANSWER 12 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
 AN 2000339230 EMBASE  
 TI Selection of **tumor-specific internalizing** human antibodies from phage libraries.  
 AU Poul M.-A.; Becerril B.; Nielsen U.B.; Morisson P.; Marks J.D.  
 CS J.D. Marks, Depts. Anesthesia/Pharmaceut. Chem., University of California, San Francisco General Hospital, 1001 Potrero Avenue, San Francisco, CA 94110, United States. marksj@anesthesia.ucsf.edu  
 SO Journal of Molecular Biology, (1 Sep 2000) 301/5 (1149-1161).  
 Refs: 50  
 ISSN: 0022-2836 CODEN: JMOBAK  
 CY United Kingdom  
 DT Journal; Article  
 FS 029 Clinical Biochemistry  
 LA English  
 SL English

L14 ANSWER 35 OF 51 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
 AN 2000:25390 SCISEARCH  
 GA The Genuine Article (R) Number: 269VX  
 TI Assessment of novel anti-pl85(HER-2) monoclonal antibodies for **internalization**-dependent therapies  
 AU Park J H M; Yang X W; Park J J; Press O W; Press M F (Reprint)  
 CS UNIV SO CALIF, KENNETH NORRIS JR COMPREHENS CANC CTR, BREAST CANC RES PROGRAM, 1441 EASTLAKE AVE, LOS ANGELES, CA 90033 (Reprint); UNIV SO CALIF, KENNETH NORRIS JR COMPREHENS CANC CTR, BREAST CANC RES PROGRAM, LOS ANGELES, CA 90033; UNIV SO CALIF, KENNETH NORRIS JR COMPREHENS CANC CTR, DEPT PATHOL, LOS ANGELES, CA 90033; UNIV WASHINGTON, SCH MED, DEPT BIOL STRUCT, SEATTLE, WA 98195; UNIV WASHINGTON, SCH MED, DEPT MED, SEATTLE, WA 98195; FRED HUTCHINSON CANC RES CTR, SEATTLE, WA 98195  
 CYA USA  
 SO HYBRIDOMA, (DEC 1999) Vol. 18, No. 6, pp. 487-495.  
 Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538.  
 ISSN: 0272-457X.  
 DT Article; Journal

FS LIFE  
LA English  
REC Reference Count: 40  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L14 ANSWER 36 OF 51 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
AN 95:45653 SCISEARCH  
GA The Genuine Article (R) Number: PY896  
TI CHIMERIZATION OF LL2, A RAPIDLY **INTERNALIZING** ANTIBODY SPECIFIC  
FOR B-CELL LYMPHOMA  
AU LEUNG S O (Reprint); SHEVITZ J; PELLEGRINI M C; DION A S; SHIH L B;  
GOLDENBERG D M; HANSEN H J  
CS IMMUNOMEDICS INC, MORRIS PLAINS, NJ, 07950 (Reprint); CTR MOLEC MED &  
IMMUNOL, GARDEN STATE CANC CTR, NEWARK, NJ, 07103  
CYA USA  
SO HYBRIDOMA, (DEC 1994) Vol. 13, No. 6, pp. 469-476.  
ISSN: 0272-457X.  
DT Article; Journal  
FS LIFE  
LA ENGLISH  
REC Reference Count: 46  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

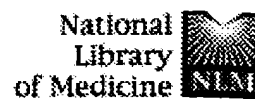
L14 ANSWER 41 OF 51 CANCERLIT on STN  
AN 96646809 CANCERLIT  
DN 96646809  
TI **Cancer** therapy with antibody-cytotoxic agent conjugates (Meeting  
abstract).  
AU Mountain A  
CS Dept of Oncology Biology, Celltech Limited, 216 Bath Road, Slough, SL1  
4EN, UK.  
SO Hum Antibodies Hybridomas, (1995) 6 (1) .  
ISSN: 0956-860X.  
(MEETING ABSTRACTS)  
DT English  
LA English  
FS Institute for Cell and Developmental Biology  
EM 199607  
ED Entered STN: 19970509  
Last Updated on STN: 19970509

L14 ANSWER 42 OF 51 CANCERLIT on STN  
AN 96605944 CANCERLIT  
DN 96605944  
TI Chimeras, castor beans, and **cancer**: antibody and ligand-toxin  
conjugates as therapeutic agents.  
AU Griffin T W; Recht L; Maher E; Delichatsios H; Raso V  
CS University of Massachusetts Medical Center, Worcester, MA.  
SO Non-serial, (1994) Molecular and Immunologic Approaches. Huber  
BE, Carr BI., eds. (Cancer Therapy in the Twenty-First Century, Vol I)  
Mount Kisco, NY, Futura Publishing, p.227-73, 1994. .  
DT Book; (MONOGRAPH)  
LA English  
FS Institute for Cell and Developmental Biology  
EM 199605  
ED Entered STN: 19970509  
Last Updated on STN: 19970509

L14 ANSWER 43 OF 51 CANCERLIT on STN  
AN 96604587 CANCERLIT

DN 96604587  
TI Specific targeting of **tumor** vascular endothelium antigen  
(endosialin) using radiolabeled monoclonal antibody FB5 (Meeting  
abstract).  
AU Lee F T; Scott A; Cebon J; Rettig W J; Welt S; Old L J  
CS Tumor Targeting Program, Ludwig Inst. for Cancer Research, Austin Hosp.,  
Heidelberg, Victoria 3084, Australia.  
SO J Immunother, (1994) 16 (2) 151.  
ISSN: 1053-8550.  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Institute for Cell and Developmental Biology  
EM 199605  
ED Entered STN: 19970509  
Last Updated on STN: 19970509

L14 ANSWER 45 OF 51 CANCERLIT on STN  
AN 96192698 CANCERLIT  
DN 96192698 PubMed ID: 8621884  
TI An enzymatic method to determine receptor-mediated endocytosis.  
AU Cobern L; Selvaraj P  
CS Department of Pathology, Emory University, Atlanta, GA 30322, USA.  
NC AI R29 30632 (NIAID)  
SO JOURNAL OF BIOCHEMICAL AND BIOPHYSICAL METHODS, (1995 Nov) 30  
(4) 249-55.  
Journal code: 7907378. ISSN: 0165-022X.  
CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS MEDLINE; Priority Journals  
OS MEDLINE 96192698  
EM 199606  
ED Entered STN: 19960710  
Last Updated on STN: 19970509



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<a href="#">#8</a>	Search #6 AND (cancer or tumor* or carcin* ) Field: Title/Abstract, Limits: Publication Date to 2000/10/18	16:05:06	<a href="#">131</a>
<a href="#">#7</a>	Search #4 AND (phage-display or "phage display") Field: Title/Abstract, Limits: Publication Date to 2000/10/18	16:00:15	<a href="#">6</a>
<a href="#">#6</a>	Search #4 AND (select* or identif* ) Field: Title/Abstract, Limits: Publication Date to 2000/10/18	15:59:45	<a href="#">938</a>
<a href="#">#5</a>	Search internaliz* AND (antibod*) Field: Title/Abstract, Limits: Publication Date to 2000/10/18	15:59:23	<a href="#">2098</a>
<a href="#">#4</a>	Search internaliz* AND (peptid* or ligand or antibod*) Field: Title/Abstract, Limits: Publication Date to 2000/10/18	15:59:12	<a href="#">4470</a>
<a href="#">#3</a>	Search internaliz* AND (peptid* or ligand or antibod*)	15:58:48	<a href="#">7046</a>
<a href="#">#2</a>	Search internaliz\$ AND (peptid* or ligand or antibod*)	15:58:23	<a href="#">0</a>
<a href="#">#1</a>	Search internaliz\$ and (peptid* or ligand or antibod*)	15:58:17	<a href="#">0</a>

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Oct 28 2004 14:51:27